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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,417	11/04/2003	Alfred Binggeli	21477	5814

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HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
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EXAMINER

STOCKTON, LAURA

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 08/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/700,417

Applicant(s)

BINGGELI ET AL.

Examiner

Laura L. Stockton, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-56 is/are pending in the application.
- 4a) Of the above claim(s) 51 and 54-56 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12, 16-20, 22-26, 29-35, 39-44, 46, 47, 50, 52 and 53 is/are rejected.
- 7) ☒ Claim(s) 13-15, 21, 27, 28, 36-38, 45, 48 and 49 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 1-56 are pending in the application.

Election/Restrictions

Applicants' election with traverse of Group I, and the species of Example 47 on page 67 (named below), in the reply filed on January 10, 2005 was acknowledged in the previous Office Action.

Example 47

a) [rac]-3-{4-[2-(2-tert-Butyl-5-methyl-oxazol-4-yl)-ethoxy]-2-methyl-phenyl}-2-ethoxy-propionic acid ethyl ester

[0176] In analogy to the *Mitsunobu*-procedure described in example 1, step f, [rac]-2-ethoxy-3-(4-hydroxy-2-methyl-phenyl)-propionic acid ethyl ester (example 46 b)) was reacted with 2-(2-tert-butyl-5-methyl-oxazol-4-yl)-ethanol (example 1, step e)) in the presence of triphenylphosphine and di-tert-butyl azodicarboxylate to yield [rac]-3-{4-[2-(2-tert-butyl-5-methyl-oxazol-4-yl)-ethoxy]-2-methyl-phenyl}-2-ethoxy-propionic acid ethyl ester as colorless oil.

MS: 440.4 (M+Na)⁺, 418.4 (M+H)⁺, 374.4, 349.4, 282.3, 226.3.

b) [rac]-3-{4-[2-(2-tert-Butyl-5-methyl-oxazol-4-yl)-ethoxy]-2-methyl-phenyl}-2-ethoxy-propionic acid

The requirement was deemed proper and made FINAL in the previous Office Action.

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Claims 51 and 54-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions. Applicant timely traversed the restriction (election) requirement in the reply filed on January 10, 2005.

Rejections made in the previous Office Action that do not appear below have been overcome. Therefore, arguments pertaining to these rejections will not be addressed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1-12, 16-20, 22-26, 29-35, 39-44, 46, 47, 50, 52 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hulin {WO 91/19702}, taken alone, or in combination with the teachings of Brooks et al. {WO 02/16331}.

*Determination of the scope and content of the prior art (MPEP
§2141.01)*

Applicants claim oxazole compounds. Hulin teaches oxazole compounds that are structurally similar to the instant claimed compounds. See in Hulin (pages 6-7), for example, Formula (II) wherein Z is alkyl; Z¹ is alkyl; X is O; Y is N; m is 2; W is O; ----- represents no bond; X¹ is O; R is alkyl; and Y¹ is hydroxy. Also note Example 13 on page 39.

*Ascertainment of the difference between the prior art and the claims
(MPEP §2141.02)*

The difference between the compounds of Hulin and the instant claimed compounds is that of a hydrogen (in the teaching of Hulin) versus a homolog such as a

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methyl group (instant R³-R⁶ variables, note proviso) attached to the phenyl ring in instant formula (I).

Finding of prima facie obviousness--rational and motivation (MPEP

§2142-2413)

To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). Additionally, it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., a hypoglycemic agent).

Alternatively, Brooks et al. teach the interchangeability of hydrogen versus an alkyl group on said phenyl ring in hypoglycemic agents. See in Brooks et al. the definition of the Y variable on page 4 (e.g., unsubstituted or substituted phenylene); the possible substituents on the phenylene found on page 6, lines 28-30; the use on page 5; and especially Example 14 on page 83.

The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in Hulin, or alternatively, especially in view of the teachings of Brooks et al., to arrive at the instant claimed compounds with the expectation of obtaining compounds which could be used as hypoglycemic agents. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Response to Arguments

Applicants' arguments filed May 31, 2005 have been considered. Applicants argue that a *prima facie* case of obviousness has not been established because there is absolutely no motivation to modify Hulin to obtain the compounds of the instant invention. Applicants argue that there is no motivation to modify the compounds of Hulin because: (1) all the generic structures and species in Hulin (and in Brooks et al.) are extremely broad and/or different; and (2) the utilities or properties of the compounds disclosed in Hulin and the claimed invention are different.

In response, Applicants' arguments have been considered but have not been found persuasive. Hulin teaches oxazole compounds that are structurally similar to the instant claimed compounds. See in Hulin (pages 6-7), for example, Formula (II) wherein Z is alkyl; Z¹ is alkyl; X is O; Y is N; m is 2; W is O; -----

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represents no bond; X¹ is O; R is alkyl; and Y¹ is hydroxy. Especially note Example 13 on page 39.

Further, Hulin teach that their oxazole compounds are useful as, hypocholesterolemic agents (page 1, lines 5-9), one of the same utilities Applicants disclose. See paragraph [0039] on page 14 and paragraph [0044] on page 16 of the instant specification. Additionally, there is no requirement that the prior art must suggest that the claimed product will have the same or similar utility as that discovered by applicant in order to support a legal conclusion of obviousness. In re Dillon, 16 U.S.P.Q. 2d 1897, 1904 (Fed. Cir. 1990). Therefore, there is sufficient motivation to modify the compounds of Hulin.

Applicants argue that: (1) the compounds of Formula (I) in Hulin are structurally different; (2) 1/12 or 8.3% of the compounds embraced by formula (II) in Hulin relate to oxazoles; (3) the central phenyl moiety of the compounds of Hulin are unsubstituted whereas in the

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instant claimed compounds the central phenyl moiety is substituted; (4) the variables in Hulin (i.e., R, X, Y, Z, etc.) are much different and/or extremely broad; and (5) Brooks et al. disclose a very broad and different generic structure.

In response, firstly, Formula (I) in Hulin was not relied upon in making the rejection of the instant claims under 35 USC 103. Secondly, the total number of specific specie prepared in a prior art reference is not a determining factor in establishing a *prima facie* case of obviousness. It is well established that consideration of a reference is not limited to the preferred embodiments or working examples, but extends to the entire disclosure for what it fairly teaches, when viewed in light of the admitted knowledge in the art, to person of ordinary skill in the art. In re Boe, 148 USPQ 507, 510 (CCPA 1966).

Thirdly, and as stated above, the difference between the compounds of Hulin and the instant claimed

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compounds is that of a hydrogen (in the teaching of Hulin) versus a homolog such as a methyl group (instant R^3 - R^6 variables, note proviso) attached to the phenyl ring in instant formula (I) in claim 1. Fourth and fifthly, although the disclosures in Hulin and Brooks et al. may be perceived as broad to Applicants, the motivation to prepare additional compounds embraced by Hulin lies in the fact that both Hulin and Brooks et al. prepare specie which differ from the instant claimed compounds at only one or two positions (see Example 13 on page 39 in Hulin and Example 14 on page 83 in Brooks et al.). If not for this difference in each of the prior art references specifically prepared specie, the instant claims would have also been rejected under 35 USC 102(b).

Applicants argue that: (1) there are no teachings of similar properties or uses in Hulin and the presently claimed invention because the instant claimed compounds bind to and activate the peroxisome

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proliferator activated receptors PPAR-alpha and PPAR-gamma; and (2) proper motivation to combine the teachings of Hulin and Brooks et al. has not been established.

All of Applicants' arguments have been considered but have not been found persuasive. As stated above, there is no requirement that the prior art must suggest that the claimed product will have the same or similar utility as that discovered by applicant in order to support a legal conclusion of obviousness. In re Dillon, 16 U.S.P.Q. 2d 1897, 1904 (Fed. Cir. 1990). Applicants are arguing the mode of action. However, the same end result and the same patients are being treated by Hulin and by the method disclosed by Applicants in the instant specification (i.e., treating patients having high cholesterol levels). Therefore, Applicants' arguments are not persuasive.

Applicants argue that there is no motivation to combine the teachings of Hulin and Brooks et al. This

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argument is not persuasive. The test for combining references is not what individual references themselves suggest but rather what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. In re McLaughlin, 170 USPQ 209 (1971).

Each of Hulin (pages 6-7) and Brooks et al. (pages 4-5) teach oxazole compounds that are structurally similar to the instant claimed compounds and each other. Each of Hulin (page 19, starting at line 31, thru to page 23) and Brooks et al. (page 5, lines 4-14) teach that their oxazole compounds are useful in treating, for example, high cholesterol levels. Brooks et al. even teach that their compounds are peroxisome proliferator activated receptor agonists (page 1, lines 9-23). For all the reasons given above, the instant claimed invention would have been suggested to one skilled in the art.

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The elected species of Example 47 is not allowable over the art of record.

Allowable Subject Matter

Claims 13-15, 21, 27, 28, 36-38, 45, 48 and 49 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the

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mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for

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unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

A handwritten signature in black ink, appearing to read 'Laura L. Stockton', written over a horizontal line.

Laura L. Stockton, Ph.D.

Patent Examiner

Art Unit 1626, Group 1620

Technology Center 1600

August 15, 2005